Preparation and pyrolysis of 1-(pyrazol-5-yl)-1,2,3-triazoles and related compounds[1]

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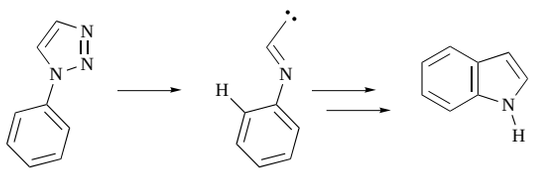
1-(Pyrazol-5-yl)-1,2,3-triazoles 8a, 9a and 10 are prepared by cycloaddition of 5-azidopyrazoles with methyl prop-2-ynoate. The regiochemistry of the process is confirmed by synthesis of 9a using an authentic route from ethyl 2-formyl-2-diazoacetate 13. Flash vacuum pyrolysis of 8a, 9a and 10 gives 5-methoxypyrazolo[1,5-*a*]pyrimidin-7-ones 16–18 by a mechanism involving an unexpected oxoketenimine–imidoyl ketene rearrangement as the key step. The mechanism is supported by a ^{13}C labelling experiment. A general route to pyrazolo[1,5-*a*]pyrimidin-7-ones from pyrazolylaminomethylene Meldrum's acid derivatives (*e.g.* 30–32) is also reported.

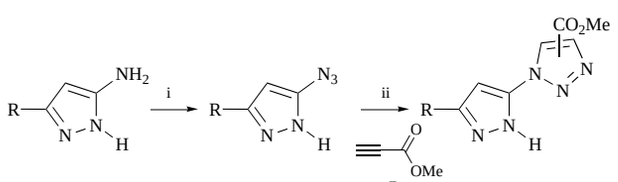
The formation of indoles by photolysis or pyrolysis of 1-aryl-1,2,3-triazoles is well known[2,3] (Scheme 1), and the present



Scheme 1

study was initiated in an attempt to extend the methodology to the preparation of fused heterobicyclic five-membered ring systems including imidazopyrazoles. In the event, an unexpected rearrangement took place[1] leading to pyrazolopyrimidinone systems *via* an oxoketenimine–imidoyl ketene interconversion. We now present full details of this work, certain aspects of which have been reinvestigated recently by Fulloon and Wentrup.[4]

5-Aminopyrazoles **1**–**3** are readily available, and can be easily transformed to the corresponding azido derivatives **4**–**6** in 46–99% yield by diazotisation and treatment with sodium azide.[5] We therefore investigated the cycloaddition of these azides with electron-deficient alkynes as the initial route to the key 1-(pyrazol-5-yl)triazole precursors (Scheme 2). It was necessary



1 R = H
2 R = Bu^t
3 R = Ph

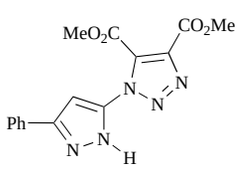
4 R = H
5 R = Bu^t
6 R = Ph

8 R = H
9 R = Bu^t
10 R = Ph

Scheme 2 *Reagents and conditions*: i, $NaNO_2$, HCl, then NaN_3; ii, heat

to select conditions which were sufficiently mild to avoid the thermal degradation of the azide. Thus cycloaddition of the azides **4** and **5** with methyl prop-2-ynoate **7** occurred smoothly in refluxing toluene (110 °C) and the triazoles **8** (86%) and **9** (79%), respectively, precipitated from solution as *ca.* 5:1 mixtures of regioisomers (see below). Although the 3-phenyl derivative **6** decomposed under these conditions, cycloaddition with **7** was successfully accomplished in boiling acetonitrile solution (81°C) and only a single isomer **10** precipitated in 45% yield. After purification, the triazoles **8**–**10** were obtained with water (or solvent) of crystallisation.

Dimethyl acetylenedicarboxylate reacted with 5-azido-3-phenylpyrazole **6** in refluxing acetonitrile to give the triazole **11** (30%), but other dipolarophiles such as ethyl phenylprop-2-ynoate, phenylacetylene, phenyl vinyl sulfoxide and ethyl trimethylsilylprop-2-ynoate were of insufficient reactivity to compete with azide decomposition (see Experimental section). Similarly, 2-azidoimidazole **12** did not react cleanly with methyl prop-2-ynoate **7** in refluxing toluene.



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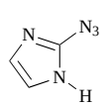

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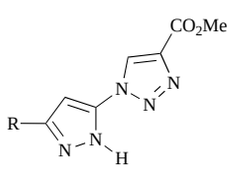
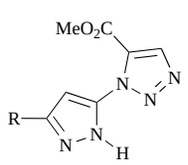


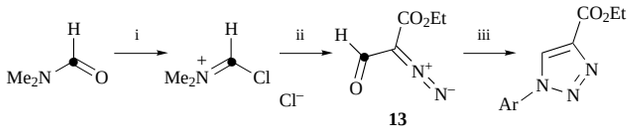
8a R = H
9a R = Bu^t
10 R = Ph



8b R = H
9b R = Bu^t

It is known that cycloaddition of arylazides with electron-deficient alkynes generally favours the configuration found in the adducts **8a** and **9a**, although often the regioselectivity is low.[6,7] The major adducts **8**–**10** are clearly related structurally, since the triazole protons show similar high frequency chemical shifts (δ_H 9.18–10.17); the corresponding resonances of the minor isomers (where present) occur at much lower frequency (*e.g.* **8b** δ_H 8.44). An attempted NOE experiment to prove the regiochemistry was unsuccessful and so it was necessary to develop an unambiguous synthetic route. A possible route was reported almost 30 years ago by Stojanovic and Arnold,[8] who showed that ethyl 2-formyl-2-diazoacetate **13**, which can be

made in two steps from *N*,*N*-dimethylformamide, reacts with aniline derivatives to give ethyl 1-aryl-1,2,3-triazole-4-carboxylates in good yield (Scheme 3). Thus when **13** was



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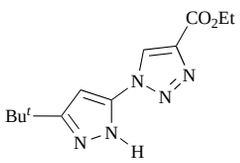
● = ^{13}C (for synthesis of **9a***)

Scheme 3 *Reagents and conditions*: i, $(COCl)_2$; ii, EtO_2CCHN_2; iii, $ArNH_2$

reacted overnight with 5-amino-3-*tert*-butylpyrazole **2** in ethanol containing some acetic acid, the triazole **14** was obtained in 81% yield. This compound showed the triazole proton resonance at δ_H 10.12, which clearly shows that the major product of the cycloaddition is the adduct **9a** as expected. This was further confirmed by an ester exchange reaction of **14** in methanol containing sodium methoxide to give a compound in 98% yield which was identical with **9a**.



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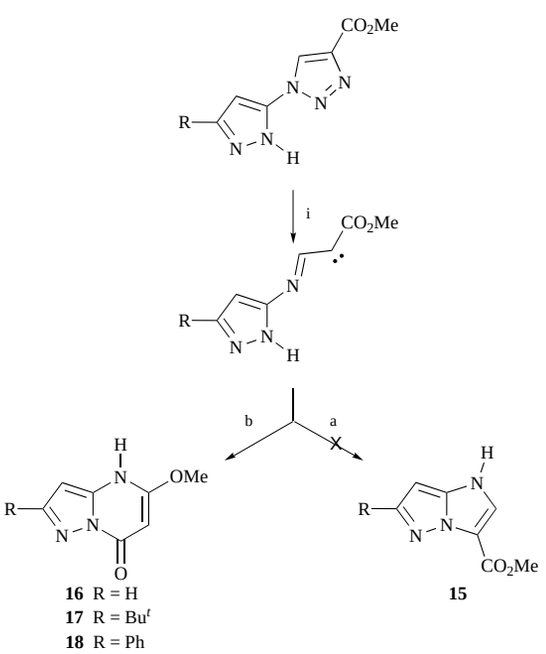
The pyrazole ring protons show similar chemical shifts for both regioisomers. In addition, there is an indication from the magnitude of $^3J_{HH}$ in the pyrazole rings of **8a** and **8b** (*ca*. 1.9 Hz) that both isomers may exist in solution as the 1*H*-tautomer shown, possibly due to intramolecular hydrogen bonding with the 2-nitrogen atom of the triazole ring.

The 1,2,3-triazoles **8a**, **9a** and **10a** were pyrolysed under FVP conditions at 600 °C (10^{-2}–10^{-3} Torr) and clean single products condensed in each case at the exit point of the furnace. The mass spectra of these materials showed the correct molecular ion expected for loss of dinitrogen from the triazoles, followed by the expected cyclisation to the imidazo[1,2-*b*]pyrazole system **15** (Scheme 4, route a). The product from pyrolysis of the



16 R = H
17 R = Bu^t
18 R = Ph

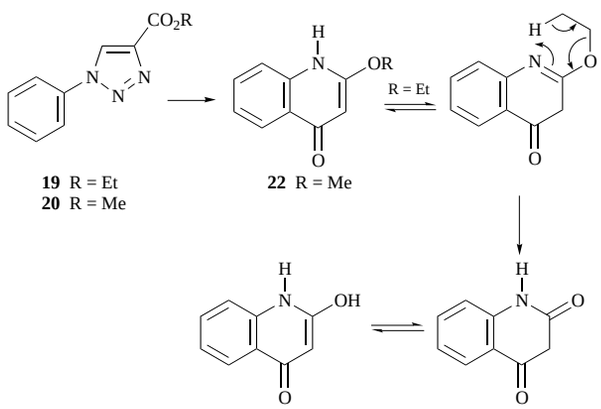
15

Scheme 4 *Reagents and conditions*: i, FVP, 600 °C, 0.001 Torr

parent system **8a** still showed two sets of doublets (^3J 1.8 Hz) which confirmed that any cyclisation could not have taken place onto the 4-position of the pyrazole. The remaining proton (derived from the triazole ring) resonated at δ_H 5.26. However, the IR spectra of the pyrolysis products surprisingly showed no ester carbonyl stretch in the range 1715–1800 cm^{-1}. In addition, the chemical shift of the proton at the 2-position of authentic 6-methylimidazo[1,2-*b*]pyrazole[9] is δ_H 6.95; it is inconceivable that an adjacent ester substituent could cause a *low* frequency shift of nearly 1.7 ppm, and so the imidazo[1,2-*b*]pyrazole system **15** was ruled out as the product from the pyrolyses.

An NOE experiment on the product of the pyrolysis of the phenyl derivative **10** showed enhancement of the methoxy signal (4%) on irradiation of the peak at δ_H 5.31 and *vice versa* (8%); these effects are also much larger than would be expected if the methoxy group had been part of an ester substituent, and imply that the methoxy group is close in space to the proton at δ_H 5.31. Irradiation of the *ortho* protons of the phenyl group showed only the expected enhancements of the *meta* protons (12%) and the adjacent proton derived from the pyrazole ring (18%), and so the connectivity of this portion of the molecule has not been affected by the pyrolysis.

The 5-methoxypyrazolo[1,5-*a*]pyrimidin-7-one structures **16**–**18** are consistent with these observations (Scheme 4, route b); in particular the position of the electron-donating methoxy substituent adjacent to the isolated proton (6-position) explains the results of the NOE experiments and the low frequency resonance of this proton. The formation of this structure requires that a skeletal rearrangement of the non-pyrazolic portion of the molecule has occurred. This was confirmed by synthesis and pyrolysis (600 °C, 10^{-3} Torr) of ethyl 1-phenyl-1,2,3-triazole-4-carboxylate[8] **19** (Scheme 5), which gave the quinolone **21**, iden-



19 R = Et
20 R = Me

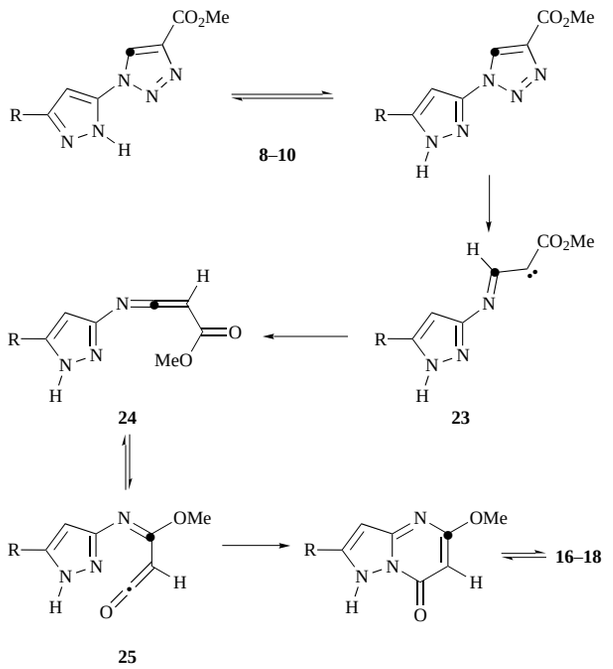
22 R = Me

21

Scheme 5

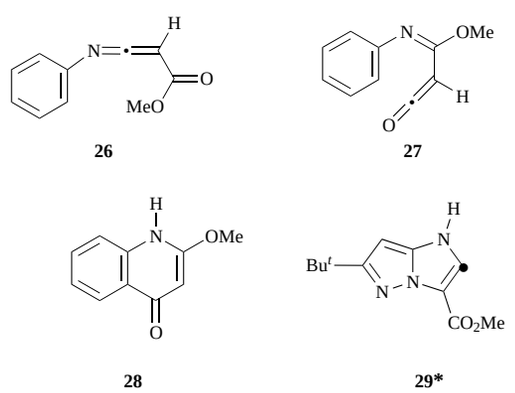
tical in all respects with a commercially available authentic sample. The dealkylation of the ethoxy group may occur as a subsequent thermal process by a *cis*-elimination mechanism (Scheme 5), which is well known for 2-alkoxypyridines and related compounds.[10] However, the corresponding methyl ester **20** has been recently pyrolysed by Fulloon and Wentrup,[4] and the expected methoxyquinolone **22** was isolated as the major product, particularly at high temperatures.

To account for the formation of **16**–**18** the mechanism shown in Scheme 6 was proposed.[1] An equivalent scheme can account for the formation of the quinolone **22**. The first step involves the well precedented[2,3] formation of the imidoyl carbene **23**, followed by its insertion into the adjacent C–H bond to generate the ketenimine carboxylic ester **24**. Such insertions are well known in general in gas-phase carbene chemistry[11] and the 1,2-shift in imidoyl carbenes in particular is also known.[12] In an attempt to circumvent this step of the mechanism, the 5-substituted triazole **11** was pyrolysed, but although extrusion of nitrogen was noted by the rise in pressure in the vacuum line, no useful products were isolated.



Scheme 6

The key step of the rearrangement is the methoxy migration in the ketenimine **24** to give the imidoyl ketene **25**. Facile 1,3-shifts of thioalkoxy groups on this energy surface have been reported[13] and, subsequent to our preliminary communication,[1] Fulloon and Wentrup have identified both the ketenimine **26** and the imidoyl ketene **27** (related to **24** and **25**, respectively) *en route* to the quinolone **28** by matrix isolation.[4] This step of the mechanism is therefore secure.

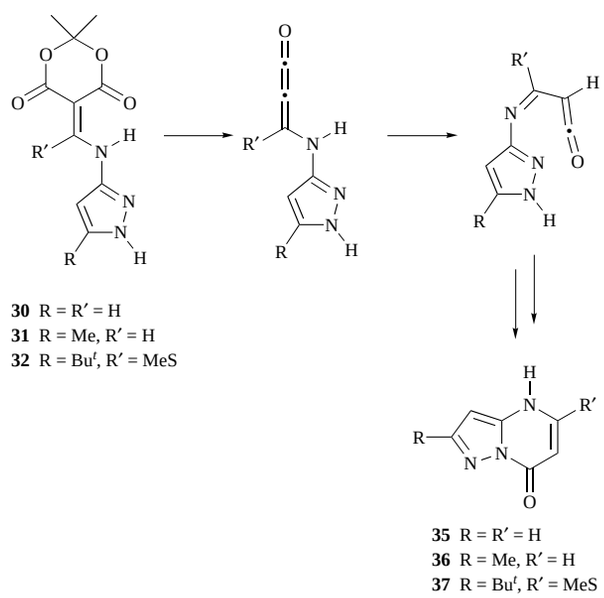


26 **27** **28** **29***

The overall effect of the 1,2-H shift and the 1,3-MeO shift is that the original triazole methine carbon atom (C-5) becomes the quaternary carbon (also C-5) in the product, and we sought to prove this by a ^{13}C labelling experiment involving the precursor **9a***. This was made by reaction of the aminopyrazole **2** with labelled formyldiazoacetate ester (Scheme 3, labelled atoms highlighted) which was itself derived from dimethyl-[^{13}C]formamide. Before the pyrolysis, it was first necessary to assign unambiguously the quaternary carbon atoms in a product, and the phenyl derivative **18** was chosen for detailed study. The five signals in question occur at δ_C 160.80, 157.20, 152.72, 140.41 and 132.67; the last appeared as a triplet in the ^{1}H-coupled spectrum, and is due to the ipso carbon atom of the phenyl group. Similarly, the bridgehead carbon atom (C-3a) would be expected to occur as a doublet due to coupling to H-3, and this was observed at δ_C 140.41. The corresponding position of the signal at δ_C 152.72 in compounds **16** and **17** was highly substituent dependent, and is therefore due to C-2. The peak at δ_C 157.20 appeared as a singlet in the ^{1}H-coupled spectrum and was assigned as the carbonyl carbon atom, since $^2J_{CH}$ of such atoms in 6-membered ring enone systems may be expected to be insignificant.[14] The remaining resonance at δ_C 160.80 was therefore assigned as due to the 5-position; in agreement with this interpretation, the corresponding signal of the known quinolone **22** (R=Me) appears at δ_C 160.5.[15]

When the ^{13}C labelled precursor **9*** was pyrolysed under identical conditions to those of its unlabelled analogue, the only enhanced signal in the ^{13}C NMR spectrum of the pyrolysate was that due to the quaternary C-5 (δ_C 160.92) of **17***, in agreement with the mechanism of Scheme 6. In the particular pyrolysis, a minor peak was also observed at δ_C 165.01 which is due to an unidentified impurity. This is unlikely to be the imidazo[1,2-*b*]pyrazole **29***, since the C-2 resonance in this system generally occurs at δ_C < 120.[16]

The final step of the mechanism (Scheme 6) involves regiospecific cyclisation of the ketene intermediate **25** to the final product. An alternative route to this energy surface was developed by pyrolysis of the Meldrum's acid derivatives **30**–**32** which were obtained from the appropriate aminopyrazoles and either methoxymethylene Meldrum's acid **33** or the ketene thioacetal **34** by standard methods (see Experimental section). FVP of **30**–**32** at 600 °C generated methylene ketene intermediates which isomerise by 1,3-H shift to the imidoyl ketenes. As expected, these cyclise to the pyrazolo[1,5-*a*]pyrimidin-7-ones **35**–**37** in *ca.* 50% yield with no trace of isomeric products (Scheme 7). Examples of this ring system have been investigated

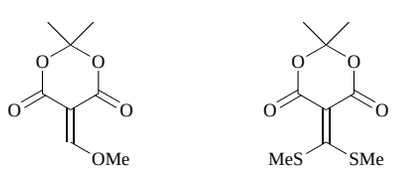


30 R = R′ = H
31 R = Me, R′ = H
32 R = Bu^t, R′ = MeS

35 R = R′ = H
36 R = Me, R′ = H
37 R = Bu^t, R′ = MeS

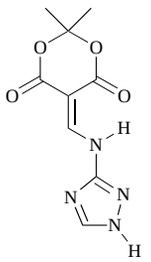
Scheme 7

as anti-inflammatory agents,[17] and the present route provides a convenient alternative synthesis.



33 **34**

As an extension of this part of the work, the aminotriazole derivative **38** was also pyrolysed, and two isomeric triazolopyrimidinones **39** and **40** which could not be separated by chromatography were obtained in 76% overall yield. Surprisingly, the proportion of these products was temperature dependent, with one component (36% of the mixture at 400 °C) rising to 69% at 700 °C, with a corresponding change in the percentage of the other component. Identification of the isomers was made by



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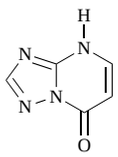

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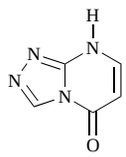

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^{13}C NMR spectroscopy, since it is know that the chemical shift of the free 'triazole' ring carbon atom is dishielded by *ca.* 20 ppm in the [1,5-*a*] isomer **39** relative to the alternative [4,3-*a*] isomer **40**.[18] The spectrum of the mixture obtained from a 700 °C pyrolysis showed two major and two minor CH peaks in the range δ_C 133–153, due to the 'triazole' carbon atoms and the carbon atoms adjacent to the NH of the six-membered ring. These were distinguished by a fully-coupled ^{13}C NMR spectrum of the mixture. Thus the 'triazole' CHs occurred as simple doublets with large one-bond coupling constants at δ_C 151.93 (major, ^1J 209.0 Hz) and 133.23 (minor, ^1J 222.8 Hz), whereas the six-membered ring carbon atoms resonated as a doublet of doublets at δ_C 140.60 (major, ^1J 183.6, ^2J 3.3 Hz) and as a broad doublet at δ_C 148.20 (minor, ^1J 180.8 Hz) with rather smaller coupling constants. The 'triazole' CHs are indeed separated by *ca.* 20 ppm; the major (thermodynamic) product at 700 °C has the more deshielded 'triazole' carbon atom and is therefore identified as the [1,5-*a*] isomer **39**. Hence the kinetic product **40** is formed by cyclisation onto the 4-position of the initial 'triazole'.

Experimental

^{1}H and ^{13}C NMR spectra were recorded at 200 and 50 MHz respectively for solutions in [^{2}H]chloroform unless otherwise stated. Coupling constants (*J*) are quoted in Hz.

Preparation of azides. General method[5]

The appropriate amine (10 mmol) was dissolved in hydrochloric acid (5 M, 15 cm^3) and cooled to < 0 °C. A solution of sodium nitrite (0.76 g, 11 mmol) dissolved in water (5 cm^3, cooled to < 0 °C) was added and the mixture was stirred for 5–10 min. A solution of sodium azide (0.98 g, 15 mmol) in water (5 cm^3) was cautiously added and the mixture was left to stir (at < 0 °C) for a further 30 min; a precipitate usually formed in the reaction vessel. The mixture was extracted with dichloromethane (3 × 25 cm^3) and the organic extracts were dried over magnesium sulfate. The dichloromethane was removed *in vacuo* to give the azide as a solid which was pure enough for further use and characterisation.

5-Azidopyrazole 4. From 5-aminopyrazole **1** (0.504 g, 46%), mp 57–58 °C (lit.,[5] 60 °C); ν_{max}/cm^{-1} 2130.

5-Azido-3-*tert*-butylpyrazole 5. From 5-amino-3-*tert*-butylpyrazole **2** (1.63 g, 99%), mp 94–95 °C (HRMS: Found M$^+$, 165.1003. $C_7H_4N_5$ requires *M*, 165.1014); ν_{max}/cm^{-1} 2125; δ_H 12.54 (1H, br s), 5.84 (1H, s) and 1.34 (9 H, s); δ_C 156.87 (q), 146.26 (q), 92.16, 31.55 (q) and 29.70; *m/z* 165 (M$^+$, 51%), 137 (14), 108 (38), 94 (43), 81 (42) and 67 (100).

5-Azido-3-phenylpyrazole 6. From 5-amino-3-phenylpyrazole **3** (1.77 g, 96%), mp 147–148 °C (HRMS: Found M$^+$, 185.0703. $C_9H_7N_5$ requires *M*, 185.0701); ν_{max}/cm^{-1} 2120; δ_H([$^2H_6$]acetone) 7.79–7.73 (2H, m), 7.50–7.33 (3H, m) and 6.64 (1H, s); δ_C([$^2H_6$]acetone) 147.65 (q), 144.15 (q), 128.11, 127.72, 124.35 and 92.13, one quaternary absent; *m/z* 185 (M$^+$, 48%), 159 (4), 157 (6), 129 (20), 128 (90), 102 (100) and 77 (43).

2-Azidoimidazole. From 2-aminoimidazole sulfate (0.35 g, 64%), mp 138 °C (decomp.) [lit.,[19] 140 °C (decomp.)]; ν_{max}/cm^{-1} 2122.

Methyl 1-(1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate 8

A solution of 5-azidopyrazole **4** (1.42 g, 13 mmol) and methyl prop-2-ynoate **7** (1.7 g, 1.8 cm^3, 20 mmol) in toluene (7 cm^3) was heated to reflux under a nitrogen atmosphere for 2.5 h. On cooling a brown precipitate was formed, which was found to be a 4.6:1 mixture of two isomers (2.16 g, 86%, both isomers). Crystallisation from acetic acid gave the major isomer *methyl* 1-(1H-*pyrazol*-5-*yl*)-1H-1,2,3-*triazole*-4-*carboxylate* **8a**, mp 254–255 °C (from acetic acid) (Found: C, 43.4; H, 3.9; N, 35.3. $C_7H_7N_5O_2$·0.1 CH_3CO_2H requires C, 43.4; H, 3.6; N, 35.2%); δ_H([$^2H_6$]DMSO) 13.38 (1H, br s), 9.18 (1H, s), 7.99 (1H, m), 6.79 (1H, m) and 3.87 (3H, s); δ_C([$^2H_6$]DMSO) 160.37 (q), 145.12 (q), 138.92 (q), 131.40, 126.68, 97.06 and 51.89; *m/z* 193 (M$^+$, 17%), 164 (11), 162 (17), 135 (12), 134 (100), 133 (21), 107 (36) and 106 (42).

The minor isomer methyl 1-(1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-5-carboxylate **8b** was identified by NMR spectroscopy; δ_H([$^2H_6$]DMSO) 8.44 (1H, s), 7.96 (1H, unresolved from major isomer), 6.64 (1H, m) and 3.78 (3H, s); δ_C([$^2H_6$]DMSO) 157.54 (q), 143.93 (q), 136.93, 130.43, 129.64 (q), 101.54 and 52.54.

Methyl 1-(3-*tert*-butyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate 9a

5-Azido-3-*tert*-butylpyrazole **5** (0.687 g, 4.16 mmol) and methyl prop-2-ynoate **7** (0.70 g, 8.33 mmol) were dissolved in toluene (5 cm^3) and the reaction mixture was heated to reflux for 3 h under a nitrogen atmosphere. The mixture was cooled and a yellow precipitate was isolated. The crude product (79%) was recrystallised from ethyl acetate to give *methyl* 1-(3-tert-*butyl*-1H-*pyrazol*-5-*yl*)-1H-1,2,3-*triazole*-4-*carboxylate* **9a** (0.72 g, 70%), mp 192–193 °C (from ethyl acetate) (Found: C, 53.0; H, 6.1; N, 28.1. $C_{11}H_{15}N_5O_2$ requires C, 53.0; H, 6.05; N, 28.1%); δ_H 10.17 (1H, s), 6.65 (1H, s), 4.06 (3H, s) and 1.42 (9H, s) (NH signal not apparent); δ_C 162.65 (q), 155.71 (q), 145.78 (q), 139.36 (q), 126.59, 92.87, 52.56, 31.28 (q) and 29.78; *m/z* 249 (M$^+$, 51%), 220 (40), 218 (18), 206 (100), 190 (94), 179 (32), 174 (70) and 150 (18).

The minor (5-carboxylate) isomer **9b** was identified from the ^{1}H NMR spectrum of the mixture; δ_H 8.25 (1H, s), 6.40 (1H, s), 3.85 (3H, s) and 1.38 (9H, s).

Methyl 1-(3-phenyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate 10

A solution of 5-azido-3-phenylpyrazole **6** (0.37 g, 2 mmol) and methyl prop-2-ynoate **7** (0.351 g, 0.372 cm^3, 4.2 mmol) in acetonitrile (6 cm^3) was heated to reflux under a nitrogen atmosphere for 4 h. On cooling a white precipitate was obtained. This was identified as *methyl* 1-(3-*phenyl*-1H-*pyrazol*-5-*yl*)-1H-1,2,3-*triazole*-4-*carboxylate* **10** (0.24 g, 45%), mp 254–255 °C (from ethanol) (Found: C, 57.2; H, 4.15; N, 25.0. $C_{13}H_{11}N_5O_2$·0.25H_2O requires C, 57.05; H, 4.2; N, 25.6%); δ_H([$^2H_6$]DMSO) 13.85 (1H, br s), 9.22 (1H, s), 7.87–7.42 (5H, m), 7.27 (1H, s) and 3.88 (3H, s); δ_C([$^2H_6$]DMSO) 160.35 (q), 145.39 (q), 144.37 (q), 138.97 (q), 129.09, 128.98, 128.12 (q), 126.64, 125.33, 94.68 and 51.94; *m/z* 269 (M$^+$, 46%), 240 (62), 238 (14), 210 (100), 198 (23), 183 (37) and 170 (17).

Dimethyl 1-(3-phenyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4,5-dicarboxylate 11

A solution of 5-azido-3-phenylpyrazole **6** (0.37 g, 2 mmol) was dissolved in acetonitrile (5 cm^3). Dimethyl acetylenedicarboxylate (0.284 g, 0.246 cm^3, 2 mmol) was added and the mixture, under a nitrogen atmosphere, was heated to reflux for 8 h. On cooling a white precipitate formed which was identified as *dimethyl* 1-(3-*phenyl*-1H-*pyrazol*-5-*yl*)-1H-1,2,3-*triazole*-4,5-*dicarboxylate* **11** (0.200 g, 30%), mp 195–196 °C (from acetic acid) (Found: C, 54.2; H, 4.1; N, 21.2. $C_{15}H_{13}N_5O_4$·0.2H_2O requires C, 54.45; H, 4.05; N, 21.2%); δ_H([$^2H_6$]DMSO) 7.89–7.85 (2H, m), 7.56–7.43 (3H, m), 7.33 (1H, s), 3.96 (3H, s) and 3.91 (3H, s); δ_C([$^2H_6$]DMSO) 159.55 (q), 159.39 (q), 144.92 (q),

144.82 (q), 137.10 (q), 131.37 (q), 129.33, 128.09, 125.64, 95.74, 54.13 and 52.78 (1 quarternary absent); *m/z* 327 (M^+, 21%), 268 (29), 267 (100), 224 (12), 209 (20) and 185 (15).

Reactions of 5-azido-3-*tert*-butylpyrazole 5 with other dienophiles

5-Azido-3-*tert*-butylpyrazole **5** (0.33 g, 2 mmol) was dissolved in toluene (5–10 cm^3) and reacted with the following dienophiles under various conditions.

With ethyl phenylprop-2-ynoate (0.348 g, 2 mmol) the mixture was heated to reflux for 4 h. Removal of solvent *in vacuo* yielded only decomposition products.

With phenylacetylene (0.202 g, 2 mmol), the mixture was heated to reflux for 5 h. Reduced pressure evaporation of solvent only yielded starting material and decomposition products.

With phenyl vinyl sulfoxide (0.450 g, 3 mmol) the mixture was heated to reflux for 5 h. Removal of solvent *in vacuo* yielded decomposition products.

With ethyl (trimethylsilyl)prop-2-ynoate (0.485 g, 2.5 mmol) the mixture was heated to reflux for 12 h. Removal of solvent gave an intractable mixture.

Reaction of 2-azidoimidazole 12 and methyl prop-2-ynoate 7

2-Azidoimidazole **12** (0.350 g, 2 mmol) was treated with methyl prop-2-ynoate **7** (0.566 g, 0.60 cm^3, 6.7 mmol) in toluene. The mixture was heated to reflux for 3 h during which time a brown precipitate formed which was found to be polymeric material. Removal of solvent yielded decomposition products.

Ethyl 2-formyl-2-diazoacetate 13[8]

Prepared by the literature method from *N*,*N*-dimethylchloromethaniminium chloride (4.18 g, 32.5 mmol) and ethyl diazoacetate (3.74 g, 3.44 cm^3, 32.5 mmol) (added *via* syringe pump) in dry chloroform (12 cm^3) at −8 °C under a nitrogen atmosphere, the product (1.10 g, 30%) was purified by Kugelrohr distillation, bp 81–82 °C/10 Torr (lit.,[8] 82–83 °C/10 Torr); δ_H 9.54 (1H, s), 4.22 (2H, q, ^3J 7.1) and 1.22 (3H, t, ^3J 7.1); δ_C 181.10, 160.83 (q), 61.56 and 13.86 (one quaternary absent).

Ethyl 1-phenyl-1*H*-1,2,3-triazole-4-carboxylate 19[8]

Ethyl 2-formyl-2-diazoacetate **13** (0.426 g, 3 mmol) was dissolved in ethanol (3 cm^3). A solution of aniline (0.27 g, 2.9 mmol) in ethanol (1.8 cm^3) and acetic acid (0.6 cm^3) was added and the mixture was stirred at room temperature for 16 h. On removal of solvent a solid was obtained, and crystallisation from ethanol gave white needles of ethyl 1-phenyl-1*H*-1,2,3-triazole-4-carboxylate **19** (0.450 g, 70%), mp 86–87 °C (lit.,[8] 88 °C).

Ethyl 1-(3-*tert*-butyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate 14, and its conversion to the methyl ester 9a

5-Amino-3-*tert*-butylpyrazole **2** (0.278 g, 2 mmol) was dissolved in ethanol (1.2 cm^3) and acetic acid (0.4 cm^3). A solution of ethyl 2-formyl-2-diazoacetate **13** (0.284 g, 2 mmol) in ethanol (2 cm^3) was added and the mixture was stirred for 16 h. On removal of solvent, a yellow solid was obtained, which was identified as *ethyl* 1-(3-tert-*butyl*-1H-*pyrazol*-5-*yl*)-1H-1,2,3-*triazole*-4-*carboxylate* **14** (0.427 g, 81%), mp 155–156 °C (from cyclohexane–ethyl acetate) (Found: C, 54.7; H, 6.35; N, 25.95. $C_{12}H_{17}N_5O_2 \cdot 0.1H_2O$ requires C, 54.5; H, 6.5; N, 26.4%); δ_H 10.12 (1H, s), 6.63 (1H, s), 4.55 (2H, q, ^3J 7.1), 1.47 (3H, t, ^3J 7.1) and 1.41 (9H, s); δ_C 162.32 (q), 155.64 (q), 145.75 (q), 139.61 (q), 126.61, 92.78, 61.95, 31.28 (q), 29.79 and 14.07; *m/z* 263 (M^+, 44%), 220 (84), 190 (100), 174 (59), 164 (50), 163 (86) and 148 (79).

Ethyl 1-(3-*tert*-butyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate (0.263 g, 1 mmol) was treated with a solution of sodium methoxide [from sodium (0.05 g)] in methanol (5 cm^3). The mixture was stirred at room temperature for 3 h, poured into water and neutralised with dilute hydrochloric acid. The solution was extracted with dichloromethane (3 × 10 cm^3) and the extracts were dried over magnesium sulfate. Removal of solvent gave methyl 1-(3-*tert*-butyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylate **9a** (0.238 g, 98%), identical in all respects with that prepared by cycloaddition.

Pyrolysis of methyl 1-(1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylates

The triazoles were sublimed at 1×10^{-3} Torr into a horizontal silica furnace tube (35 × 2.5 cm), which was maintained at a temperature of 600 °C by an electrical heater. The quantity of precursor, inlet temperature and pyrolysis time of the FVP experiments are indicated in parentheses. The products condensed at the exit point of the furnace and were recovered from the trap by scraping with a spatula. They were glassy in appearance and could not be successfully purified by crystallisation.

The unsubstituted compound **8a** (0.170 g, inlet 130 °C, 45 min) gave 5-*methoxy*-4,7-*dihydropyrazolo*[1,5-a]*pyrimidin*-7-*one* **16** (0.060 g, 42%), mp 203–205 °C (HRMS: Found M^+, 165.0538. $C_7H_7N_3O_2$ requires *M*, 165.0538); δ_H([$^2H_6$]DMSO) 7.78 (1H, d, ^3J 1.8), 5.98 (1H, d, ^3J 1.8), 5.26 (1H, s) and 3.90 (3H, s); δ_C([$^2H_6$]DMSO) 161.19 (q), 157.33 (q), 142.16, 139.79 (q), 88.50, 75.10 and 56.51; *m/z* 165 (M^+, 100%), 164 (22), 134 (24), 122 (13), 107 (22) and 106 (11).

The 3-*tert*-butyl derivative **9a** (0.71 g, inlet 140 °C, 3 h) gave 2-tert-*butyl*-5-*methoxy*-4,7-*dihydropyrazolo*[1,5-a]*pyrimidin*-7-*one* **17** (0.350 g, 50%), mp 207–209 °C (HRMS: Found M^+, 221.1155. $C_{11}H_{15}N_3O_2$ requires *M*, 221.1164); δ_H([$^2H_6$]DMSO) 5.86 (1H, s), 5.20 (1H, s), 3.88 (3H, s) and 1.27 (9H, s); δ_C([$^2H_6$]DMSO) 163.79 (q), 160.88 (q), 157.25 (q), 139.88 (q), 85.15, 75.02, 56.55, 32.22 (q) and 29.87; *m/z* 221 (M^+, 96%), 220 (40), 206 (100), 179 (40) and 174 (30).

The 3-phenyl derivative **10** (0.168 g, inlet 160 °C, 2 h) gave 5-*methoxy*-2-*phenyl*-4,7-*dihydropyrazolo*[1,5-a]*pyrimidin*-7-*one* **18** (0.080 g, 53%), mp 167–169 °C (HRMS: Found M^+, 241.0850. $C_{13}H_{11}N_3O_2$ requires *M*, 241.0851); δ_H([$^2H_6$]DMSO) 7.97–7.92 (2H, m), 7.51–7.38 (3H, m), 6.45 (1H, s), 5.31 (1H, s) and 3.92 (3H, s); δ_C([$^2H_6$]DMSO) 160.80 (q), 157.20 (q), 152.72 (q), 140.41 (q), 132.67 (q), 128.63 (2C), 125.93, 85.45, 75.35 and 56.85; *m/z* 241 (M^+, 100), 240 (22), 227 (9), 213 (14), 212 (13), 210 (11), 198 (15), 173 (16) and 159 (16).

Dimethyl 1-(3-phenyl-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4,5-dicarboxylate **11** (0.051 g, inlet 155 °C, 1 h 15 min) gave a mixture which showed at least four spots by TLC, and so this pyrolysis was not pursued further.

Pyrolysis of ethyl 1-phenyl-1*H*-1,2,3-triazole-4-carboxylate 19

FVP of the ethyl ester (0.083 g) at 600 °C (1×10^{-3} Torr, inlet temperature 130 °C) for 1 h gave a product which was identified as quinoline-2,4-diol as its 4-keto tautomer **21**, by comparison with an authentic sample whose δ_H values are quoted in square brackets after the corresponding pyrolysate values; δ_H([$^2H_6$]-DMSO) 11.22 (1H, s) [11.24 (1H, s)], 7.78 (1H, d, ^3J 7.9) [7.78 (1H, d, ^3J 8.0)], 7.53–7.44 (1H, m) [7.53–7.45 (1H, m)], 7.28–7.09 (2H, m) [7.29–7.09 (2H, m)] and 5.75 (1H, s) [5.76 (1H, s)]; δ_C([$^2H_6$]DMSO) 163.72 (q), 162.58 (q), 139.27 (q), 130.95, 122.76, 121.19, 115.26, 115.22 (q) and 98.32.

^{13}C Isotopic labelling experiment

Dimethyl[^{13}C]formamide (0.250 g) was reacted with oxalyl chloride (0.428 cm^3) to give *N*,*N*-dimethylchloro[^{13}C]-methaniminium chloride (0.436 g) as previously described.[20] The salt was then reacted with ethyl diazoacetate (0.710 cm^3) under the conditions described above to give ethyl 2-[^{13}C]formyl-2-diazoacetate **13*** (0.116 g). Ethyl 2-[^{13}C]formyl-2-diazoacetate (0.071 g) was then reacted with 5-amino-3-*tert*-butylpyrazole **2** (0.069 g) to give, after ester exchange (Na–MeOH), methyl 1-(3-*tert*-butyl-1*H*-pyrazol-5-yl)-1*H*-[5-^{13}C]-1,2,3-triazole-4-carboxylate **9a*** (0.046 g, 41%); δ_C([$^2H_6$]-acetone) 124.24 {δ_C([^{2}H]chloroform) 126.59, isotopically enhanced}. Pyrolysis of **9a*** (0.028 g, 140 °C, 1 h) at 600 °C returned 2-*tert*-butyl-5-methoxy-4,7-dihydro[5-^{13}C]pyrazolo-[1,5-*a*]pyrimidin-7-one **17***; δ_C([$^2H_6$]DMSO) 160.92 (q) (iso-

topically enriched). An unidentified impurity peak was recorded at δ 165.01.

2,2-Dimethyl-1,3-dioxane-4,6-diones 30, 31 and 38

The appropriate amino compound (5 mmol) and 5-methoxymethylene-2,2-dimethyl-1,3-dioxane-4,6-dione[21] **33** (0.93 g, 5 mmol) were dissolved in acetonitrile (25 cm^3) and the solution was stirred at room temperature for 15 min. The precipitate which formed was filtered to give the product.

5-(*N*-Pyrazol-3-ylaminomethylene)-2,2-dimethyl-1,3-dioxane-4,6-dione 30. From 3-aminopyrazole (1.18 g, 95%), mp 195–196 °C (from ethanol) (Found: C, 50.2; H, 4.6; N, 17.6. $C_{10}H_{11}N_3O_4$ requires C, 50.6; H, 4.65; N, 17.7%); δ_H 11.30 (1H, br s), 8.75 (1H, s), 7.56 (1H, d, ^3J 2.5), 6.23 (1H, d, ^3J 2.5) and 1.74 (6H, s); δ_C 165.11 (q), 163.56 (q), 153.31, 148.11 (q), 130.33, 104.99 (q), 94.43, 86.91 (q) and 26.86; *m/z* 237 (M^+, 12%), 179 (29), 161 (100) and 107 (22).

5-[*N*-(5-Methylpyrazol-3-yl)aminomethylene]-2,2-dimethyl-1,3-dioxane-4,6-dione 31. From 3-amino-5-methylpyrazole (1.15 g, 92%), mp 188–189 °C (from ethanol) (Found: C, 52.7; H, 5.4; N, 16.8. $C_{11}H_{13}N_3O_4$ requires C, 52.6; H, 5.2; N, 16.75%); δ_H 11.28 (1H, br s), 8.68 (1H, br s), 5.95 (1H, s), 2.31 (3H, s) and 1.73 (6H, s); δ_C 165.04 (q), 163.67 (q), 153.14, 148.29 (q), 141.20 (q), 104.89 (q), 93.49, 86.62 (q), 26.83 and 11.02; *m/z* 251 (M^+, 15%), 193 (31), 175 (100), 149 (4) and 121 (12).

5-[*N*-(1,2,4-Triazol-3-yl)aminomethylene]-2,2-dimethyl-1,3-dioxane-4,6-dione 38. From 3-amino-1,2,4-triazole (1.04 g, 86%), mp 208–209 °C (decomp., from ethanol) (Found: C, 45.3; H, 4.35; N, 23.4. $C_9H_{10}N_4O_4$ requires C, 45.4; H, 4.2; N, 23.5%); δ_H([$^2H_6$]DMSO) 14.11 (1H, br s), 11.20 (1H, br s), 8.75 (1H, s), 8.55 (1H, s) and 1.68 (6H, s); δ_C([$^2H_6$]DMSO) 163.88 (q), 162.32 (q), 156.28 (q), 152.37, 144.74, 104.67 (q), 87.91 (q) and 26.45; *m/z* 238 (M^+, 24%), 181 (18), 180 (93), 163 (13), 136 (35), 134 (11), 108 (100) and 81 (15).

5-{Methylthio[*N*-(5-*tert*-butylpyrazol-3-yl)amino]methylene}-2,2-dimethyl-1,3-dioxane-4,6-dione 32

5-[Bis(methylthio)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione[22] **34** (0.496 g, 2 mmol) was reacted with 5-amino-3-*tert*-butylpyrazole **2** (0.278 g, 2 mmol) in acetonitrile (4 cm^3). The mixture was first heated to reflux for 2 h and then was stirred at room temperature for a further 16 h. On removal of solvent *in vacuo* an oil was obtained; this was purified by chromatography (silica, 50:50 ethyl acetate–hexane) to give 5-{*methylthio*[N-(5-tert-*butylpyrazol*-3-*yl)amino*]*methylene}*-2,2-*dimethyl*-1,3-*dioxane*-4,6-*dione* **32** (0.234 g, 35%), mp 134–135 °C (HRMS: Found M + 1 [FAB], 340.1331. $C_{15}H_{22}N_3O_4S$ requires M + 1, 340.1331); δ_H 12.76 (1H, br s), 6.10 (1H, s), 2.34 (3H, s), 1.72 (6H, s) and 1.32 (9H, s); δ_C 177.88 (q), 163.79 (q), 155.01 (q), 145.65 (q), 103.00 (q), 96.99, 86.13 (q), 31.13 (q), 29.83, 26.19 and 18.65; *m/z* (electron impact) 281 (M^+ − 58, 33%), 263 (60), 248 (48), 237 (67), 222 (38), 221 (33) and 190 (100).

Pyrolysis reactions of 2,2-dimethyl-1,3-dioxane-4,6-diones

The compounds were pyrolysed under FVP conditions at a temperature of 600 °C and a pressure of 0.001 Torr. The products were formed at the exit of the furnace tube and were scraped out of the trap with a spatula.

The 3-aminopyrazole derivative **30** (0.500 g, inlet 120 °C, 2 h) gave 4,7-dihydropyrazolo[1,5-*a*]pyrimidin-7-one **35** (0.136 g, 48%), mp 238–240 °C (lit.,[23] 239–240 °C); δ_H([$^2H_6$]DMSO) 7.88 (1H, d, ^3J 7.3), 7.87 (1 H, d, ^3J 2.0), 6.19 (1H, d, ^3J 2.0) and 5.69 (1H, d, ^3J 7.3); δ_C([$^2H_6$]DMSO) 156.65 (q), 142.58, 141.85 (q), 139.53, 95.15 and 88.97.

The 3-amino-5-methylpyrazole derivative **31** (0.507 g, inlet 190 °C, 105 min) gave 2-methyl-4,7-dihydropyrazolo[1,5-*a*]-pyrimidin-7-one **36** (0.156 g, 52%), mp 274–277 °C (lit.,[17] 275–280 °C); δ_H([$^2H_6$]DMSO) 7.79 (1H, d, ^3J 7.3), 6.01 (1H, s), 5.62 (1H, d, ^3J 7.3) and 2.28 (3H, s); δ_C([$^2H_6$]DMSO) 156.29 (q), 151.74 (q), 142.20 (q), 138.89, 95.25, 88.64 and 13.96.

The methylthio derivative **32** [0.087 g, inlet 180 °C, 2 h, 1×10^{-4} Torr (mercury diffusion pump)] gave 2-tert-*butyl*-5-*methylthio*-4,7-*dihydropyrazolo*[1,5-a]*pyrimidin*-7-*one* **37** (0.033 g, 53%), mp 319–320 °C (HRMS: Found M^+, 237.0940. $C_{11}H_{15}N_3OS$ requires M, 237.0936); δ_H([$^2H_6$]DMSO) 5.92 (1H, s), 5.55 (1H, s), 2.57 (3H, s) and 1.29 (9H, s); δ_C([$^2H_6$]DMSO) 164.25 (q), 154.82 (q), 152.70 (q), 141.76 (q), 91.22, 84.76, 32.28 (q), 29.90 and 13.94; *m/z* 237 (M^+, 100%), 222 (23), 190 (60) and 174 (13).

The 3-aminotriazole derivative **38** (0.93 g, inlet 140 °C, 5 h) gave at 700 °C an inseparable mixture of 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one **39** (major product, see Discussion section) and 5,8-dihydro-1,2,4-triazolo[4,3-*a*]pyrimidin-5-one **40** (0.400 g, 76%) (the parameters of the minor product **40** are quoted in parentheses); δ_H([$^2H_6$]DMSO) 8.23 (1H, s) [9.05 (1H, s)], 7.98 (1H, both isomers, d, ^3J 7.4) and 5.94 (1H, d, ^3J 7.4) [5.77 (1H, d, ^3J 7.4)]; δ_C([$^2H_6$]DMSO) 156.51 (q) [156.05 (q)], 151.93 (148.20), 150.79 (q) [149.36 (q)], 140.60 (133.23) and 99.27 (96.92). When small-scale pyrolyses (0.050 g) were carried out at different furnace temperatures (400–700 °C) (inlet 140 °C, 1×10^{-3} Torr), varying proportions of the two products were obtained; ratios were determined from the integral values obtained for the peaks at δ_H 5.94 and 5.77. The relative proportions of the two isomers **40**:**39** are as follows: 400 °C, 64:36; 500 °C, 42:58; 600 °C, 36:64; 700 °C, 31:69.

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